

WHAT IS CLAIMED IS:

1. A modified antibody of class IgG wherein at least one amino acid residue from the heavy chain constant region selected from the group consisting of amino acid residues 250, 314, and 428 is different from that present in an unmodified class IgG antibody, wherein the FcRn binding affinity and/or serum half-life of said modified antibody is altered relative to that of the unmodified antibody.
- 5
2. The modified antibody according to Claim 1, wherein said unmodified class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.
- 10
3. The modified antibody according to Claim 1, wherein said unmodified class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.
4. The modified antibody according to Claim 1, wherein said unmodified class IgG antibody is a chimeric antibody, a primatized antibody, or a humanized antibody.
- 15
5. The modified antibody according to Claim 1, wherein said unmodified class IgG antibody is a human antibody.
6. The modified antibody according to Claim 1, wherein the unmodified antibody is OST577-IgG2M3 or OST577-IgG1.
- 20
7. The modified antibody according to Claim 1, wherein the unmodified antibody is Hu1D10-IgG2M3 or Hu1D10-IgG1.
8. The modified antibody according to Claim 1, wherein:
 - (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid or glutamine; or
 - 25
 - (b) said amino acid residue 428 from the heavy chain constant region is phenylalanine or leucine.
9. The modified antibody according to Claim 1, wherein amino acid residue 250 from the heavy chain constant region is glutamine.

10. The modified antibody according to Claim 1, wherein amino acid residue 428 from the heavy chain constant region is leucine.

11. The modified antibody according to Claim 1, wherein:

5 (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid and amino acid residue 428 from the heavy chain constant region is phenylalanine;

(b) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is phenylalanine; or

10 (c) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is leucine.

12. The modified antibody according to Claim 1, wherein said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is leucine.

15 13. The modified antibody according to Claim 1, wherein said amino acid residue 314 is selected from the group consisting of alanine, arginine, aspartic acid, asparagine, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine.

20 14. The modified antibody according to Claim 1, wherein said amino acid residue 314 from the heavy chain constant region is arginine.

15. The modified antibody according to Claim 1, wherein:

25 (a) said amino acid residue 250 from the heavy chain constant region is selected from the group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or

(b) said amino acid residue 428 from the heavy chain constant region is selected from the group consisting of alanine, arginine, asparagine, aspartic

acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine.

16. The modified antibody according to Claim 1, wherein said amino acid residue 250 from the heavy chain constant region is aspartic acid.
- 5 17. The modified antibody according to Claim 1, wherein said amino acid residue 428 from the heavy chain constant region is glycine.
18. The modified antibody according to Claim 1, wherein the modified antibody has a higher binding affinity for FcRn at pH 6.0 than at pH 7.4.
- 10 19. An antibody having a constant region substantially identical to that of a naturally occurring class IgG antibody wherein at least one amino acid residue from the heavy chain constant region selected from the group consisting of residues 250, 314, and 428 is different from that present in the naturally occurring class IgG antibody, wherein the FcRn binding affinity and/or serum half-life of said antibody is altered relative to the naturally occurring antibody.
- 15 20. The antibody according to Claim 19, wherein said naturally occurring class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.
- 20 21. The antibody according to Claim 19, wherein said naturally occurring class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.
22. The modified antibody according to Claim 19, wherein said naturally occurring class IgG antibody is a chimeric antibody, a primatized antibody, or a humanized antibody.
23. The antibody according to Claim 19 wherein said naturally occurring class IgG antibody is a human antibody.
- 25 24. The antibody according to Claim 19, wherein:
 - (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid or glutamine; or

(b) said amino acid residue 428 from the heavy chain constant region is phenylalanine or leucine.

25. The antibody according to Claim 19, wherein said amino acid residue 250 from the heavy chain constant region is glutamine.

5 26. The antibody according to Claim 19, wherein said amino acid residue 428 from the heavy chain constant region is leucine.

27. The antibody according to Claim 19, wherein:

10 (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid and said amino acid residue 428 from the heavy chain constant region is phenylalanine;

(b) said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is phenylalanine; or

15 (c) said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is leucine.

28. The antibody according to Claim 19, wherein said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is leucine.

20 29. The antibody according to Claim 19, wherein said amino acid residue 314 from the heavy chain constant region is selected from the group consisting of alanine, arginine, aspartic acid, asparagine, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine.

30. The antibody according to Claim 19, wherein said amino acid residue 314 from the 25 heavy chain constant region is arginine.

31. The antibody according to Claim 19, wherein:

(a) said amino acid residue 250 from the heavy chain constant region is selected from the group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or

5 (b) said amino acid residue 428 from the heavy chain constant region is selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine;

32. The antibody according to Claim 19, wherein said amino acid residue 250 from the
10 heavy chain constant region is aspartic acid.

33. The antibody according to Claim 19, wherein said amino acid residue 428 from the
heavy chain constant region is glycine.

34. A modified therapeutic or diagnostic antibody of class IgG with an *in vivo* elimination
half-life at least about 1.3-fold longer than that of the corresponding unmodified class
15 IgG antibody.

35. The modified therapeutic or diagnostic antibody of class IgG of Claim 34, wherein at
least one amino acid residue from the heavy chain constant region selected from the
group consisting of residues 250, 314, and 428 is different from that present in the
unmodified antibody.

20 36. The modified therapeutic or diagnostic antibody of class IgG of Claim 34, wherein:

(a) said amino acid residue 250 from the heavy chain constant region is
glutamic acid and amino acid residue 428 from the heavy chain constant
region is phenylalanine;

25 (b) said amino acid residue 250 from the heavy chain constant region is
glutamine and amino acid residue 428 from the heavy chain constant region
is phenylalanine; or

(c) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is leucine.

37. The modified antibody of Claim 34, wherein said amino acid residue 250 from the
5 heavy chain constant region is glutamine and said amino acid residue 428 from the
heavy chain constant region is leucine.

38. The modified antibody of Claim 34, wherein amino acid residue 428 from the heavy
chain constant region is leucine.

39. A modified therapeutic or diagnostic antibody of class IgG with an *in vivo* clearance at
10 least about 1.3-fold lower than that of the corresponding unmodified class IgG antibody.

40. The modified therapeutic or diagnostic antibody of class IgG of Claim 39, wherein at
least one of amino acid residue from the heavy chain constant region selected from the
group consisting of residues 250, 314, and 428 is different from that present in the
unmodified class IgG antibody.

15 41. The modified therapeutic or diagnostic antibody of class IgG of Claim 39, wherein

(a) said amino acid residue 250 from the heavy chain constant region is
glutamic acid and amino acid residue 428 from the heavy chain constant
region is phenylalanine;

(b) said amino acid residue 250 from the heavy chain constant region is
glutamine and amino acid residue 428 from the heavy chain constant region
is phenylalanine; or

(c) said amino acid residue 250 from the heavy chain constant region is
glutamine and amino acid residue 428 from the heavy chain constant region
is leucine.

25 42. The modified antibody of Claim 39, wherein said amino acid residue 250 from the
heavy chain constant region is glutamine and said amino acid residue 428 from the
heavy chain constant region is leucine.

43. The modified antibody of Claim 39, wherein said amino acid residue 428 from the heavy chain constant region is leucine.
44. A modified therapeutic or diagnostic antibody of class IgG with an *in vivo* area under the concentration-time curve at least about 1.3-fold higher than that of the corresponding unmodified class IgG antibody.
5
45. The modified therapeutic or diagnostic antibody of class IgG of Claim 44, wherein at least one amino acid residue from the heavy chain constant region selected from the group consisting of residues 250, 314, and 428 is different from that present in the unmodified class IgG antibody.
- 10 46. The modified therapeutic or diagnostic antibody of class IgG of Claim 44, wherein
 - (a) said amino acid residue 250 from the heavy chain constant region is glutamic acid and amino acid residue 428 from the heavy chain constant region is phenylalanine;
 - (b) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is phenylalanine; or
15
 - (c) said amino acid residue 250 from the heavy chain constant region is glutamine and amino acid residue 428 from the heavy chain constant region is leucine.
- 20 47. The modified antibody of Claim 44, wherein said amino acid residue 250 from the heavy chain constant region is glutamine and said amino acid residue 428 from the heavy chain constant region is leucine.
48. The modified antibody of Claim 44, wherein said amino acid residue 428 from the heavy chain constant region is leucine.
- 25 49. A modified antibody of class IgG derived from an unmodified antibody of class IgG wherein residue 250 from the heavy chain constant region is alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine,

isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, tryptophan, tyrosine, or valine.

50. A modified antibody of class IgG derived from an unmodified antibody of class IgG wherein residue 314 from the heavy chain constant region is alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine.
51. A modified antibody of class IgG derived from an unmodified antibody of class IgG wherein residue 428 from the heavy chain constant region is alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine.
52. A heavy chain constant region or a heavy chain Fc region of the modified antibody according to Claim 1.
- 15 53. A heavy chain constant region or a heavy chain Fc region of the antibody having a constant region substantially identical to that of a naturally occurring class IgG antibody according to Claim 19.
54. A polypeptide comprising an amino acid sequence of any one of SEQ ID NOs: 10-76.
55. A polynucleotide molecule encoding the polypeptide according to Claim 54.
- 20 56. A host cell comprising a vector comprising the polynucleotide molecule according to Claim 54.
57. A method for altering FcRn binding affinity and/or serum half-life of an antibody of class IgG comprising selecting at least one amino acid residue from the heavy chain constant region from the group consisting of residues 250, 314, and 428 and substituting the selected residue(s) with an amino acid different from that present in the unmodified antibody, thereby altering FcRn binding affinity and/or serum half-life of the antibody.

58. A method of producing a modified antibody of class IgG with an altered binding affinity for FcRn and/or an altered serum half-life as compared with the unmodified antibody comprising:

5 (a) preparing an expression vector comprising a suitable promoter operably linked to DNA encoding at least a constant region of an immunoglobulin heavy chain in which at least one amino acid residue from the heavy chain constant region selected from the group consisting of amino acid residues 250, 314, and 428 is substituted with a residue different from that present in an unmodified antibody;

10 (b) transforming host cells with said vector; and

(c) culturing said transformed host cells to produce said modified antibody.

59. The method according to Claim 58, further comprising: preparing a second expression vector comprising a promoter operably linked to DNA encoding a complementary immunoglobulin light chain and further transforming said host cells with said second expression vector.

60. The method according to Claim 58, wherein:

20 (a) said amino acid residue 250 from the heavy chain constant region is substituted with glutamic acid or glutamine; or

(b) said amino acid residue 428 from the heavy chain constant region is substituted with phenylalanine or leucine.

61. The method according to Claim 58, wherein said amino acid residue 250 from the heavy chain constant region is substituted with glutamine.

25 62. The method according to Claim 58, wherein said amino acid residue 428 from the heavy chain constant region is substituted with leucine.

63. The method according to Claim 58, wherein

(a) said amino acid residue 250 from the heavy chain constant region is substituted with glutamic acid and amino acid residue 428 from the heavy chain constant region is substituted with phenylalanine;

5 (b) said amino acid residue 250 from the heavy chain constant region is substituted with glutamine and amino acid residue 428 from the heavy chain constant region is substituted with phenylalanine; or

(c) said amino acid residue 250 from the heavy chain constant region is substituted with glutamine and amino acid residue 428 from the heavy chain constant region is substituted with leucine.

10 64. The method according to Claim 58, wherein said amino acid residue 250 from the heavy chain constant region is substituted with glutamine and said amino acid residue 428 from the heavy chain constant region is substituted with leucine.

15 65. The method according to Claim 58, wherein said amino acid residue 314 from the heavy chain constant region is substituted with a residue selected from the group consisting of alanine, arginine, aspartic acid, asparagine, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine.

66. The method according to Claim 58, wherein amino acid residue 314 from the heavy chain constant region is substituted with arginine.

20 67. The method according to Claim 58, wherein:

(a) amino acid residue 250 from the heavy chain constant region is substituted with a residue selected from a group consisting of arginine, asparagine, aspartic acid, lysine, phenylalanine, proline, tryptophan, or tyrosine; or

25 (b) amino acid residue 428 is substituted with a residue selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, lysine, proline, serine, threonine, tyrosine, or valine.

68. The method according to Claim 58, wherein said amino acid residue 250 from the heavy chain constant region is substituted with aspartic acid.
69. The method according to Claim 58, wherein said amino acid residue 428 from the heavy chain constant region is substituted with glycine.